Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Electronic Supplementary Information: Absorption behavior of doxorubicin hydrochloride in Visible region in different environments: a combined experimental and computational study

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Contents

1 Additional Informations

Table S1: The unperturbed vertical excitation energies, E_{exc}^{imp} (in water and n-hexane solutions), are reported in the second column. The unperturbed, $|\mu^{imp}|^2$, and mean perturbed $|\mu^{pert}|^2$ electronic transition dipole square length in the calculated spectra (in water and n-hexane solutions) are showed in the third and fourth columns respectively. The shift between the unperturbed and the (mean) perturbed excitation energies, $E_{exc}^{imp} - \langle E_{exc}^{pert} \rangle$, are reported in the last column.

Transition	E_{exc}^{imp}	$\|\mu^{imp}\|^2$	$\|\mu^{pert}\|^2$	$E_{exc}^{imp} - \langle E_{exc}^{pert} \rangle$
Units	eV	$a.u.$	$a.u.$	eV
Water sol.				
$0 \longrightarrow 1$	2.59	3.06	2.08	0.11
$0 \longrightarrow 2$	2.98	0.00	0.40	0.06
$0 \longrightarrow 3$	3.19	0.52	0.42	0.14
$0 \longrightarrow 4$	3.43	0.00	0.46	0.20
$0 \longrightarrow 5$	3.66	0.06	0.09	0.25
n-hexane sol.				
Conformation A				
$0 \longrightarrow 1$	2.59	3.06	2.37	-0.08
$0 \longrightarrow 2$	2.98	0.00	0.00	-0.03
$0 \longrightarrow 3$	3.19	0.52	0.99	0.12
$0 \longrightarrow 4$	3.43	0.00	0.00	0.00
$0 \longrightarrow 5$	3.66	0.06	0.08	0.03
Conformation B				
$0 \longrightarrow 1$	2.74	1.52	2.71	0.21
$0 \longrightarrow 2$	2.86	1.18	0.05	-0.03
$0 \longrightarrow 3$	3.24	0.26	0.00	0.02
$0 \longrightarrow 4$	3.26	0.28	0.46	-0.22
$0 \longrightarrow 5$	3.81	0.01	0.22	0.10

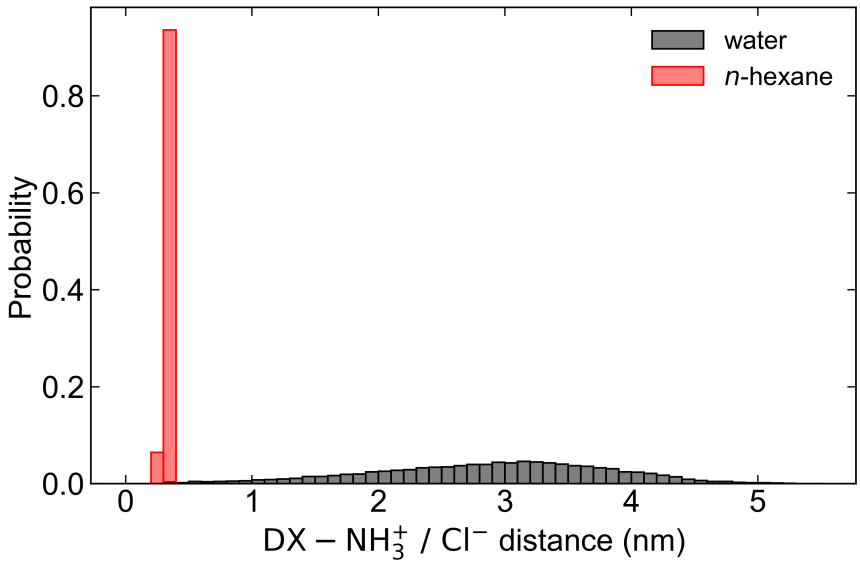

Figure S1: Distances distributions between the DX ammonium group and Cl^- ion in the MD simulations in water (black) and in *n*-hexane (red).

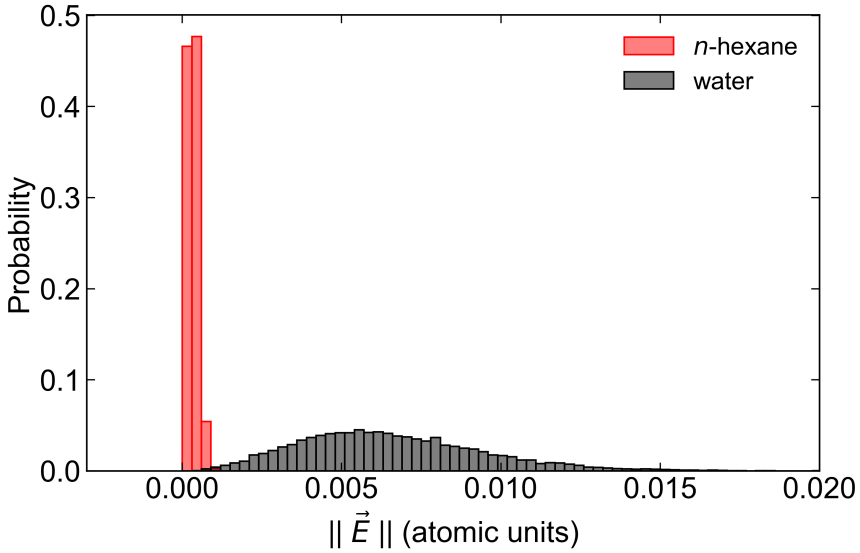

Figure S2: Probability distributions of the electric field magnitude generated by the solvent (water: black; *n*-hexane: red) along the MD simulations of DX.

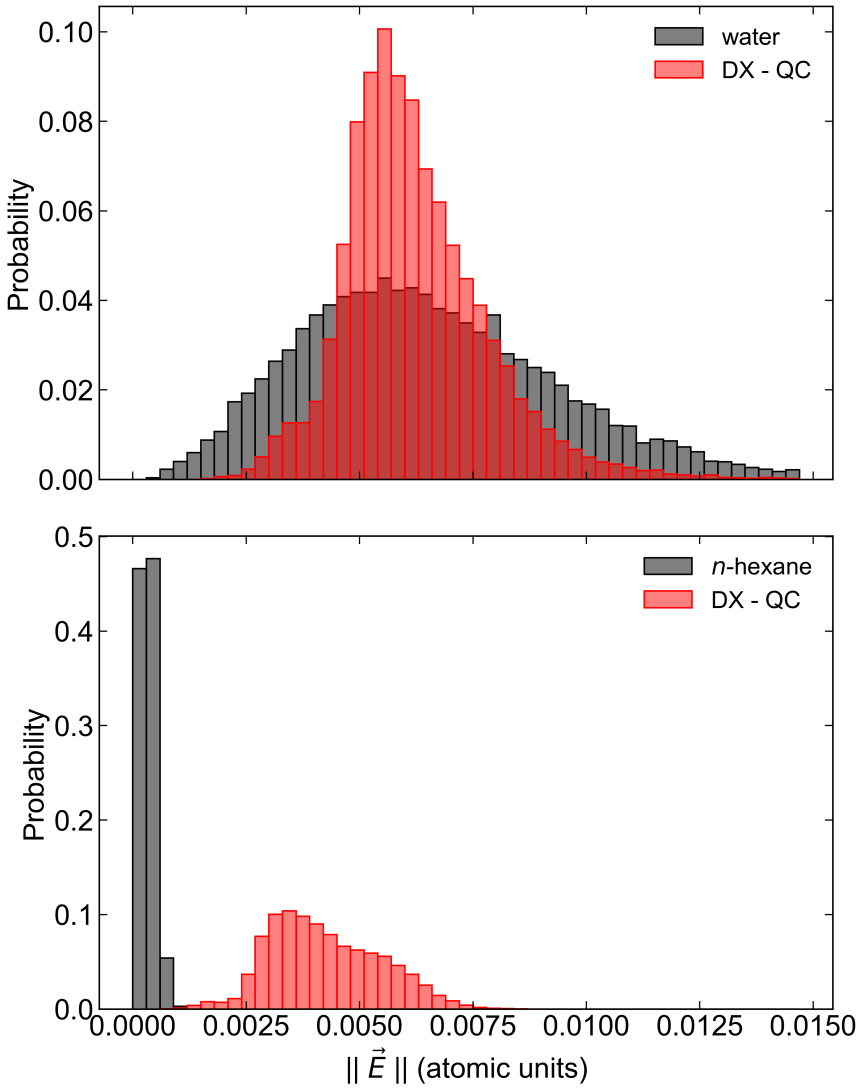

Figure S3: Probability distributions of the electric field magnitude generated by the solvent (black) and by the portion of DX not included in the QC (DX-QC; red), obtained by the MD simulations. Top: DX in water; bottom: DX in *n*-hexane. DX-QC indicates the contribution due to both the Cl^- ion and the atoms belonging to the portion of DX not included in the QC.

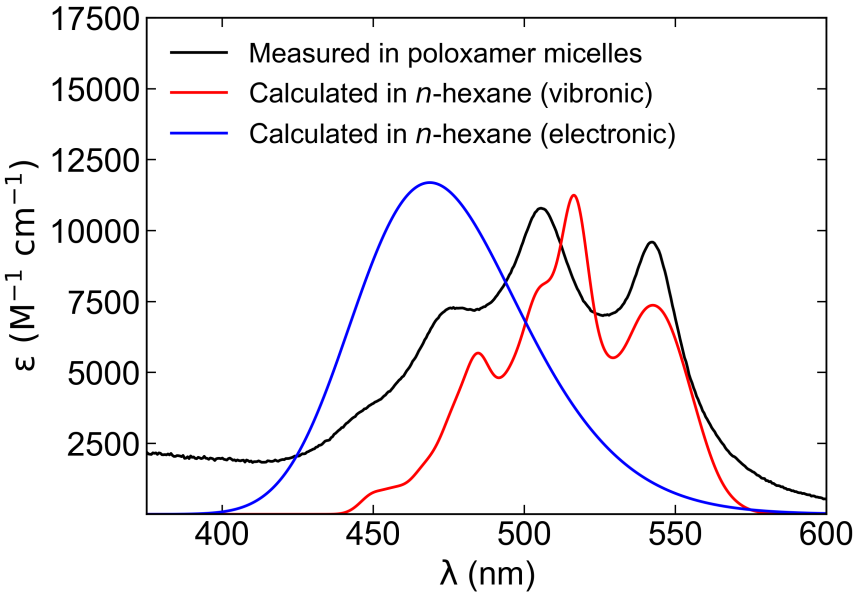

Figure S4: Calculated vertical and vibronic Vis spectra for DX in apolar environment (blue and red, respectively) in comparison with the experimental one measured in sodium cholate/F127 poloxamer mixed micelles (black).

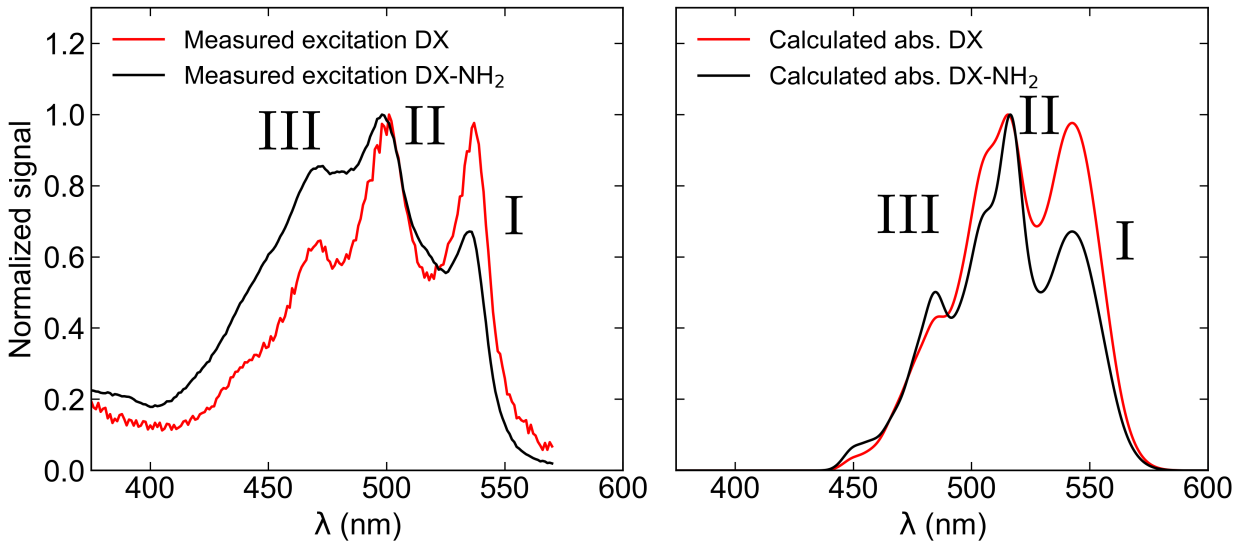

Figure S5: Fluorescence excitation spectra (left) and calculated Vis spectra (right) in *n*-hexane (both normalized) for DX in the cationic form (red) and in the neutral form (DX-NH_2; black). DX-NH_2 has been prepared from a 0.5 mM DX solution in 50 mM Tris·HCl buffer (pH= $pK_a^{NH_3^+}$ = 8.6 - pK_a value taken from[1]) stratified over chloroform and left in mild stirring overnight. 100 μL of the organic phase was then dried under vacuum and 1 mL of *n*-hexane added. After stirring and centrifuging, the surnatant was placed into a fluorescence cuvette and the excitation spectrum acquired as described in the Materials and Methods section of the main manuscript. The calculated spectra were obtained by the weighted summation of the contributions arising from the conformation A and B. The weighting factors were obtained by minimizing the differences between the predicted and measured values of the ratios of the signal intensities I and II and of the signal intensities III and II (for DX: 14% of A conformation and 86% of B conformation; for DX-NH_2: 31% of A conformation and 69% of B conformation).

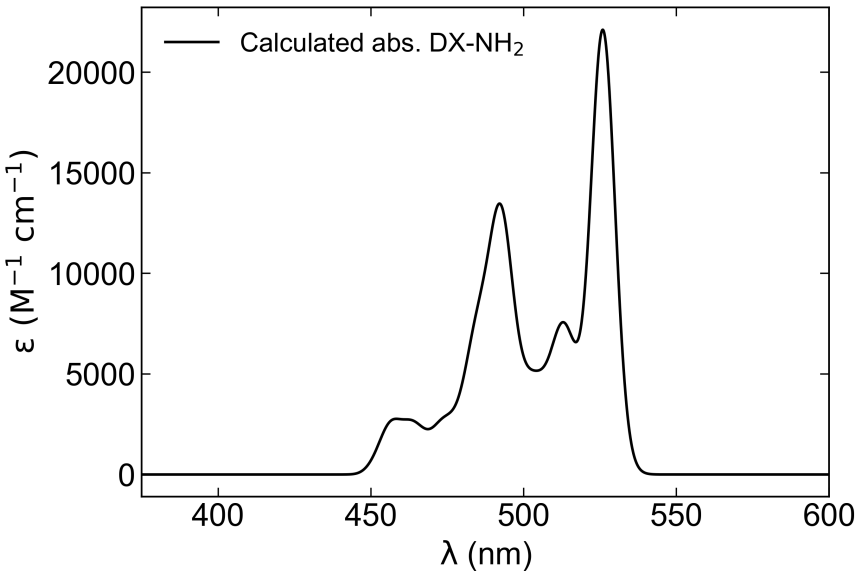

Figure S6: Calculated Vis spectrum of DX-NH_2 in *n*-hexane. It is worth noting the close analogy with the calculated Vis spectrum of DX in *n*-hexane when only the A conformer is considered (cfr. Fig. 4 in the main manuscript).

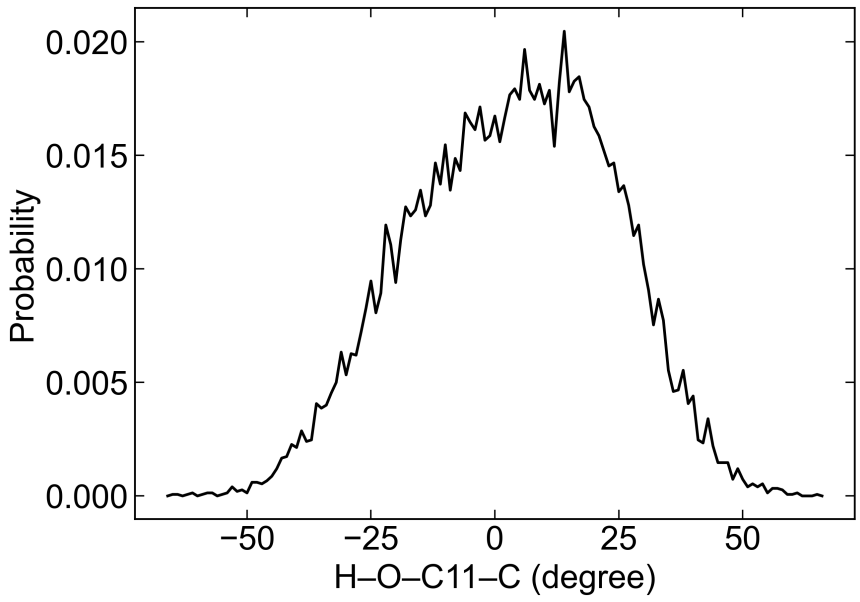

Figure S7: Probability distribution of the dihedral angle H–O–C11–C (cfr. Fig. 1 in the main manuscript for DX atom numbering) sampled during the MD simulation of DX-NH_2. It is worth to remark that only the A conformation is sampled.

Table S2: The root mean square electron-hole separation (d_{exc}) and the linear electron hole distance ($d_{e\rightarrow h}$) for the first six transitions of both A and B conformations of the QC are reported.

Transition	d_{exc} (Å)	$d_{e\rightarrow h}$ (Å)
Conformation A		
$0\longrightarrow 1$	4.25	1.58
$0\longrightarrow 2$	3.75	1.08
$0\longrightarrow 3$	4.48	2.32
$0\longrightarrow 4$	3.54	0.87
$0\longrightarrow 5$	4.12	0.07
$0\longrightarrow 6$	4.65	2.48
Conformation B		
$0\longrightarrow 1$	3.98	1.03
$0\longrightarrow 2$	3.89	0.89
$0\longrightarrow 3$	4.07	1.45
$0\longrightarrow 4$	3.98	1.31
$0\longrightarrow 5$	4.07	0.22
$0\longrightarrow 6$	4.69	2.46

2 Force Field Parameters

The following parameters for the DX and *n*-hexane molecules were obtained using ATB (Automated Topology Builder)[2] in a form which is compatible with the GROMACS software[3]. For further clarifications about the definitions of said parameters, we recommend reading the work of Schmid et al.[4].

2.1 Doxorubicin

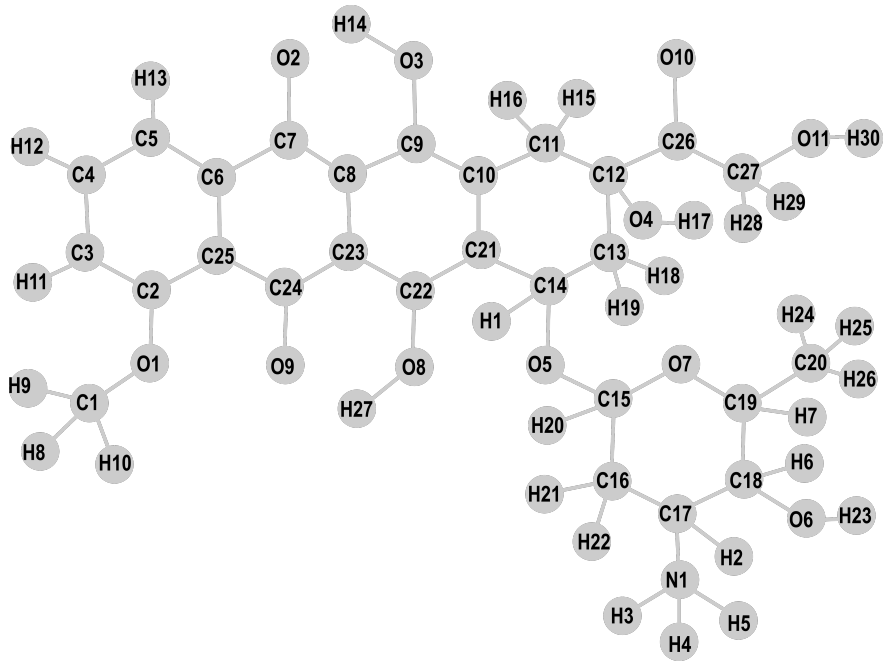

Figure S8: Atom names of the DX molecule in the force field.

Table S3: Parameters for the non bonded interactions of the DX molecule. C_6 and C_{12} are the parameters of the Lennard Jones interactions.

Index	Atom name	Atom type	Mass (Da)	Charge (e)	C_6 (kJ mol^{-1} nm^6)	C_{12} (kJ mol^{-1} nm^{12})
1	H30	H	1.0080	0.239	0	0
2	O11	OA	15.9994	-0.299	0.0022619536	$1.505529 \cdot 10^{-6}$
3	C27	C	12.0110	-0.068	0.0023406244	$4.937284 \cdot 10^{-6}$
4	H28	HC	1.0080	0.145	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
5	H29	HC	1.0080	0.091	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$

6	C26	C	12.0110	0.175	0.0023406244	$4.937284 \cdot 10^{-6}$
7	O10	O	15.9994	-0.283	0.0022619536	$1 \cdot 10^{-6}$
8	C12	C	12.0110	0.049	0.0023406244	$4.937284 \cdot 10^{-6}$
9	O4	OA	15.9994	-0.311	0.0022619536	$1.505529 \cdot 10^{-6}$
10	H17	HS14	1.0080	0.188	0.0	0.0
11	C13	C	12.0110	-0.156	0.0023406244	$4.937284 \cdot 10^{-6}$
12	H18	HC	1.0080	0.114	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
13	H19	HC	1.0080	0.116	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
14	C11	C	12.0110	-0.150	0.0023406244	$4.937284 \cdot 10^{-6}$
15	H15	HC	1.0080	0.138	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
16	H16	HC	1.0080	0.121	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
17	C10	C	12.0110	-0.042	0.0023406244	$4.937284 \cdot 10^{-6}$
18	C21	C	12.0110	-0.067	0.0023406244	$4.937284 \cdot 10^{-6}$
19	C9	C	12.0110	0.129	0.0023406244	$4.937284 \cdot 10^{-6}$
20	O3	OA	15.9994	-0.255	0.0022619536	$1.505529 \cdot 10^{-6}$
21	H14	HS14	1.0080	0.291	0.0	0.0
22	C8	C	12.0110	-0.165	0.0023406244	$4.937284 \cdot 10^{-6}$
23	C23	C	12.0110	-0.154	0.0023406244	$4.937284 \cdot 10^{-6}$
24	C22	C	12.0110	0.110	0.0023406244	$4.937284 \cdot 10^{-6}$
25	O8	OA	15.9994	-0.287	0.0022619536	$1.505529 \cdot 10^{-6}$
26	H27	HS14	1.0080	0.255	0.0	0.0
27	C24	C	12.0110	0.386	0.0023406244	$4.937284 \cdot 10^{-6}$
28	O9	O	15.9994	-0.310	0.0022619536	$1 \cdot 10^{-6}$
29	C25	C	12.0110	-0.152	0.0023406244	$4.937284 \cdot 10^{-6}$
30	C2	C	12.0110	0.152	0.0023406244	$4.937284 \cdot 10^{-6}$
31	C3	C	12.0110	-0.188	0.0023406244	$4.937284 \cdot 10^{-6}$
32	H11	HC	1.0080	0.101	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
33	C4	C	12.0110	-0.067	0.0023406244	$4.937284 \cdot 10^{-6}$
34	H12	HC	1.0080	0.154	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
35	C5	C	12.0110	-0.113	0.0023406244	$4.937284 \cdot 10^{-6}$
36	H13	HC	1.0080	0.168	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
37	C6	C	12.0110	-0.076	0.0023406244	$4.937284 \cdot 10^{-6}$
38	C7	C	12.0110	0.322	0.0023406244	$4.937284 \cdot 10^{-6}$
39	O2	O	15.9994	-0.301	0.0022619536	$1 \cdot 10^{-6}$
40	O1	OE	15.9994	-0.188	0.0022619536	$1.21 \cdot 10^{-6}$
41	C1	C	12.0110	-0.094	0.0023406244	$4.937284 \cdot 10^{-6}$

42	H8	HC	1.0080	0.094	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
43	H9	HC	1.0080	0.094	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
44	H10	HC	1.0080	0.094	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
45	C14	C	12.0110	0.093	0.0023406244	$4.937284 \cdot 10^{-6}$
46	H1	HC	1.0080	0.141	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
47	O5	OE	15.9994	-0.311	0.0022619536	$1.21 \cdot 10^{-6}$
48	C15	C	12.0110	0.195	0.0023406244	$4.937284 \cdot 10^{-6}$
49	H20	HC	1.0080	0.167	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
50	O7	OE	15.9994	-0.285	0.0022619536	$1.21 \cdot 10^{-6}$
51	C16	C	12.0110	-0.216	0.0023406244	$4.937284 \cdot 10^{-6}$
52	H21	HC	1.0080	0.118	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
53	H22	HC	1.0080	0.146	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
54	C17	C	12.0110	-0.111	0.0023406244	$4.937284 \cdot 10^{-6}$
55	H2	HC	1.0080	0.355	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
56	N1	NL	14.0067	-0.063	0.0024364096	$2.319529 \cdot 10^{-6}$
57	H3	HS14	1.0080	0.257	0.0	0.0
58	H4	HS14	1.0080	0.257	0.0	0.0
59	H5	HS14	1.0080	0.257	0.0	0.0
60	C18	C	12.0110	-0.015	0.0023406244	$4.937284 \cdot 10^{-6}$
61	H6	HC	1.0080	0.131	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
62	O6	OA	15.9994	-0.339	0.0022619536	$1.505529 \cdot 10^{-6}$
63	H23	HS14	1.0080	0.093	0.0	0.0
64	C19	C	12.0110	0.008	0.0023406244	$4.937284 \cdot 10^{-6}$
65	H7	HC	1.0080	0.122	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
66	C20	C	12.0110	-0.315	0.0023406244	$4.937284 \cdot 10^{-6}$
67	H24	HC	1.0080	0.105	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
68	H25	HC	1.0080	0.105	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
69	H26	HC	1.0080	0.105	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$

Table S4: Bond stretching parameters of the DX molecule.

Atom 1	Atom 2	Equilibrium bond length (nm)	Force constant (kJ mol^{-1} nm^{-4})
H30	O11	0.0971	$7.9547 \cdot 10^{6}$
O11	C27	0.1410	$6.5389 \cdot 10^{6}$
C27	H28	0.1130	$7.0483 \cdot 10^{6}$

C27	H29	0.1130	$7.0483 \cdot 10^{6}$
C27	C26	0.1510	$3.7279 \cdot 10^{6}$
C26	O10	0.1230	$1.6600 \cdot 10^{7}$
C26	C12	0.1530	$7.1500 \cdot 10^{6}$
C12	O4	0.1430	$8.1800 \cdot 10^{6}$
C12	C13	0.1530	$7.1500 \cdot 10^{6}$
C12	C11	0.1530	$7.1500 \cdot 10^{6}$
O4	H17	0.0971	$7.9547 \cdot 10^{6}$
C13	H18	0.1120	$3.7000 \cdot 10^{7}$
C13	H19	0.1120	$3.7000 \cdot 10^{7}$
C13	C14	0.1530	$7.1500 \cdot 10^{6}$
C11	H15	0.1130	$7.0483 \cdot 10^{6}$
C11	H16	0.1130	$7.0483 \cdot 10^{6}$
C11	C10	0.1480	$5.7300 \cdot 10^{6}$
C10	C21	0.1390	$8.6600 \cdot 10^{6}$
C10	C9	0.1430	$8.1800 \cdot 10^{6}$
C21	C22	0.1420	$3.2236 \cdot 10^{6}$
C21	C14	0.1500	$8.3700 \cdot 10^{6}$
C9	O3	0.1360	$1.0200 \cdot 10^{7}$
C9	C8	0.1400	$8.5400 \cdot 10^{6}$
O3	H14	0.0972	$1.9581 \cdot 10^{7}$
C8	C23	0.1410	$6.5389 \cdot 10^{6}$
C8	C7	0.1480	$5.7300 \cdot 10^{6}$
C23	C22	0.1390	$8.6600 \cdot 10^{6}$
C23	C24	0.1480	$5.7300 \cdot 10^{6}$
C22	O8	0.1380	$1.1000 \cdot 10^{7}$
O8	H27	0.0972	$1.9581 \cdot 10^{7}$
C24	O9	0.1250	$1.3400 \cdot 10^{7}$
C24	C25	0.1470	$8.7100 \cdot 10^{6}$
C25	C2	0.1410	$6.5389 \cdot 10^{6}$
C25	C6	0.1410	$6.5389 \cdot 10^{6}$
C2	C3	0.1410	$6.5389 \cdot 10^{6}$
C2	O1	0.1380	$1.1000 \cdot 10^{7}$
C3	H11	0.1100	$1.2100 \cdot 10^{7}$
C3	C4	0.1390	$8.6600 \cdot 10^{6}$
C4	H12	0.1100	$1.2100 \cdot 10^{7}$

C4	C5	0.1390	$8.6600 \cdot 10^6$
C5	H13	0.1100	$1.2100 \cdot 10^7$
C5	C6	0.1390	$8.6600 \cdot 10^6$
C6	C7	0.1480	$5.7300 \cdot 10^6$
C7	O2	0.1250	$1.3400 \cdot 10^7$
O1	C1	0.1430	$8.1800 \cdot 10^6$
C1	H8	0.1120	$3.7000 \cdot 10^7$
C1	H9	0.1120	$3.7000 \cdot 10^7$
C1	H10	0.1120	$3.7000 \cdot 10^7$
C14	H1	0.1130	$7.0483 \cdot 10^6$
C14	O5	0.1450	$5.2319 \cdot 10^6$
O5	C15	0.1410	$6.5389 \cdot 10^6$
C15	H20	0.1130	$7.0483 \cdot 10^6$
C15	O7	0.1420	$3.2236 \cdot 10^6$
C15	C16	0.1530	$7.1500 \cdot 10^6$
O7	C19	0.1430	$8.1800 \cdot 10^6$
C16	H21	0.1120	$3.7000 \cdot 10^7$
C16	H22	0.1120	$3.7000 \cdot 10^7$
C16	C17	0.1530	$7.1500 \cdot 10^6$
C17	H2	0.1130	$7.0483 \cdot 10^6$
C17	N1	0.1500	$8.3700 \cdot 10^6$
C17	C18	0.1560	$3.0819 \cdot 10^6$
N1	H3	0.1030	$3.2991 \cdot 10^6$
N1	H4	0.1030	$3.2991 \cdot 10^6$
N1	H5	0.1030	$3.2991 \cdot 10^6$
C18	H6	0.1130	$7.0483 \cdot 10^6$
C18	O6	0.1410	$6.5389 \cdot 10^6$
C18	C19	0.1540	$4.2166 \cdot 10^6$
O6	H23	0.0971	$7.9547 \cdot 10^6$
C19	H7	0.1130	$7.0483 \cdot 10^6$
C19	C20	0.1520	$5.4300 \cdot 10^6$
C20	H24	0.1120	$3.7000 \cdot 10^7$
C20	H25	0.1120	$3.7000 \cdot 10^7$
C20	H26	0.1120	$3.7000 \cdot 10^7$

Table S5: Angle bending parameters of the DX molecule.

Atom 1	Atom 2	Atom 3	Equilibrium angle (degree)	Force constant (kJ mol^{-1})
H30	O11	C27	109.50	450.00
O11	C27	H28	104.00	490.00
O11	C27	H29	110.30	524.00
O11	C27	C26	111.00	530.00
H28	C27	H29	109.60	450.00
H28	C27	C26	110.30	524.00
H29	C27	C26	108.53	443.00
C27	C26	O10	121.00	685.00
C27	C26	C12	120.00	560.00
O10	C26	C12	121.00	685.00
C26	C12	O4	109.50	520.00
C26	C12	C13	111.00	530.00
C26	C12	C11	111.00	530.00
O4	C12	C13	104.00	490.00
O4	C12	C11	109.50	520.00
C13	C12	C11	111.00	530.00
C12	O4	H17	109.50	450.00
C12	C13	H18	108.53	443.00
C12	C13	H19	109.50	285.00
C12	C13	C14	111.00	530.00
H18	C13	H19	107.60	507.00
H18	C13	C14	109.60	450.00
H19	C13	C14	109.00	1680.51
C12	C11	H15	108.53	443.00
C12	C11	H16	109.50	285.00
C12	C11	C10	111.00	530.00
H15	C11	H16	106.75	503.00
H15	C11	C10	108.53	443.00
H16	C11	C10	109.00	1680.51
C11	C10	C21	126.00	640.00
C11	C10	C9	120.00	560.00
C21	C10	C9	120.00	560.00
C10	C21	C22	120.00	560.00

C10	C21	C14	120.00	560.00
C22	C21	C14	120.00	560.00
C10	C9	O3	115.00	610.00
C10	C9	C8	120.00	560.00
O3	C9	C8	126.00	640.00
C9	O3	H14	109.50	450.00
C9	C8	C23	120.00	560.00
C9	C8	C7	120.00	560.00
C23	C8	C7	120.00	560.00
C8	C23	C22	120.00	560.00
C8	C23	C24	120.00	560.00
C22	C23	C24	120.00	560.00
C21	C22	C23	120.00	560.00
C21	C22	O8	115.00	610.00
C23	C22	O8	126.00	640.00
C22	O8	H27	109.50	450.00
C23	C24	O9	120.00	560.00
C23	C24	C25	120.00	560.00
O9	C24	C25	121.00	685.00
C24	C25	C2	120.00	560.00
C24	C25	C6	120.00	560.00
C2	C25	C6	120.00	560.00
C25	C2	C3	120.00	560.00
C25	C2	O1	115.00	610.00
C3	C2	O1	126.00	640.00
C2	C3	H11	120.00	505.00
C2	C3	C4	120.00	560.00
H11	C3	C4	120.00	505.00
C3	C4	H12	120.00	505.00
C3	C4	C5	120.00	560.00
H12	C4	C5	120.00	505.00
C4	C5	H13	120.00	505.00
C4	C5	C6	120.00	560.00
H13	C5	C6	120.00	505.00
C25	C6	C5	120.00	560.00
C25	C6	C7	120.00	560.00

C5	C6	C7	120.00	560.00
C8	C7	C6	120.00	560.00
C8	C7	O2	121.00	685.00
C6	C7	O2	121.00	685.00
C2	O1	C1	117.00	635.00
O1	C1	H8	103.00	420.00
O1	C1	H9	103.00	420.00
O1	C1	H10	103.00	420.00
H8	C1	H9	111.00	530.00
H8	C1	H10	111.00	530.00
H9	C1	H10	111.00	530.00
C13	C14	C21	111.00	530.00
C13	C14	H1	110.00	4763.46
C13	C14	O5	109.50	520.00
C21	C14	H1	108.00	465.00
C21	C14	O5	109.50	520.00
H1	C14	O5	111.00	530.00
C14	O5	C15	116.00	465.00
O5	C15	H20	114.00	1559.41
O5	C15	O7	106.75	503.00
O5	C15	C16	109.50	520.00
H20	C15	O7	106.00	1733.55
H20	C15	C16	111.40	532.00
O7	C15	C16	111.00	530.00
C15	O7	C19	109.50	450.00
C15	C16	H21	108.00	465.00
C15	C16	H22	108.00	465.00
C15	C16	C17	109.50	520.00
H21	C16	H22	109.60	450.00
H21	C16	C17	111.00	530.00
H22	C16	C17	111.40	532.00
C16	C17	H2	109.00	1680.51
C16	C17	N1	111.00	530.00
C16	C17	C18	109.50	520.00
H2	C17	N1	108.00	465.00
H2	C17	C18	109.00	1680.51

N1	C17	C18	109.50	520.00
C17	N1	H3	109.50	425.00
C17	N1	H4	109.50	425.00
C17	N1	H5	109.50	425.00
H3	N1	H4	109.60	450.00
H3	N1	H5	109.60	450.00
H4	N1	H5	109.60	450.00
C17	C18	H6	110.30	524.00
C17	C18	O6	109.50	520.00
C17	C18	C19	109.50	520.00
H6	C18	O6	106.00	1733.55
H6	C18	C19	109.60	450.00
O6	C18	C19	115.00	610.00
C18	O6	H23	109.50	450.00
O7	C19	C18	109.50	520.00
O7	C19	H7	109.00	1680.51
O7	C19	C20	109.50	520.00
C18	C19	H7	108.53	443.00
C18	C19	C20	111.00	530.00
H7	C19	C20	111.00	530.00
C19	C20	H24	111.00	530.00
C19	C20	H25	111.00	530.00
C19	C20	H26	111.00	530.00
H24	C20	H25	108.53	443.00
H24	C20	H26	108.53	443.00
H25	C20	H26	108.53	443.00

Table S6: Improper dihedral-angle parameters of the DX molecule.

Atom 1	Atom 2	Atom 3	Atom 4	Equilibrium improper dihedral angle (degree)	Force constant (kJ mol^{-1} rad^{-2})
C2	O1	C3	C25	0.00	167.36
C3	C2	C4	H11	0.00	167.36
C4	C3	C5	H12	0.00	167.36
C5	C4	C6	H13	0.00	167.36

C6	C5	C7	C25	0.00	167.36
C7	C6	O2	C8	0.00	167.36
C8	C7	C9	C23	0.00	167.36
C9	C8	O3	C10	0.00	167.36
C10	C9	C11	C21	0.00	167.36
C21	C10	C14	C22	0.00	167.36
C22	C21	O8	C23	0.00	167.36
C23	C8	C22	C24	0.00	167.36
C24	C23	O9	C25	0.00	167.36
C25	C2	C6	C24	0.00	167.36
C26	C12	O10	C27	0.00	167.36

Table S7: Proper dihedral angle parameters

Atom 1	Atom 2	Atom 3	Atom 4	Equilibrium proper dihedral angle (degree)	Force constant (kJ mol^{-1})	Multiplicity
H30	O11	C27	C26	0.00	1.26	3
O11	C27	C26	C12	180.00	1.00	6
O10	C26	C12	C11	0.00	1.00	6
C11	C12	O4	H17	0.00	1.26	3
C11	C12	C13	C14	0.00	5.92	3
O4	C12	C11	C10	0.00	5.92	3
C12	C13	C14	O5	0.00	5.92	3
C12	C11	C10	C9	180.00	1.00	6
C9	C10	C21	C22	180.00	41.80	2
C21	C10	C9	C8	180.00	41.80	2
C10	C21	C22	C23	180.00	41.80	2
C10	C21	C14	C13	180.00	1.00	6
C8	C9	O3	H14	180.00	16.70	2
C10	C9	C8	C23	180.00	41.80	2
C9	C8	C23	C22	180.00	41.80	2
C9	C8	C7	C6	180.00	5.86	2
C8	C23	C22	C21	180.00	41.80	2
C8	C23	C24	O9	180.00	5.86	2
C21	C22	O8	H27	180.00	16.70	2
C23	C24	C25	C2	180.00	5.86	2

C6	C25	C2	C3	180.00	41.80	2
C2	C25	C6	C5	180.00	41.80	2
C25	C2	C3	C4	180.00	41.80	2
C3	C2	O1	C1	180.00	24.00	2
C2	C3	C4	C5	180.00	41.80	2
C3	C4	C5	C6	180.00	41.80	2
C4	C5	C6	C25	180.00	41.80	2
C5	C6	C7	O2	180.00	5.86	2
C2	O1	C1	H8	0.00	1.26	3
C13	C14	O5	C15	180.00	1.00	3
C14	O5	C15	C16	180.00	1.00	3
O5	C15	O7	C19	0.00	1.26	3
O5	C15	C16	C17	0.00	5.92	3
C15	O7	C19	C18	0.00	1.26	3
C15	C16	C17	N1	0.00	5.92	3
C16	C17	N1	H3	0.00	1.05	3
C16	C17	C18	O6	0.00	5.92	3
C17	C18	O6	H23	180.00	1.00	3
C17	C18	C19	C20	0.00	5.92	3
C18	C19	C20	H24	0.00	5.92	3

2.2 *n*-hexane

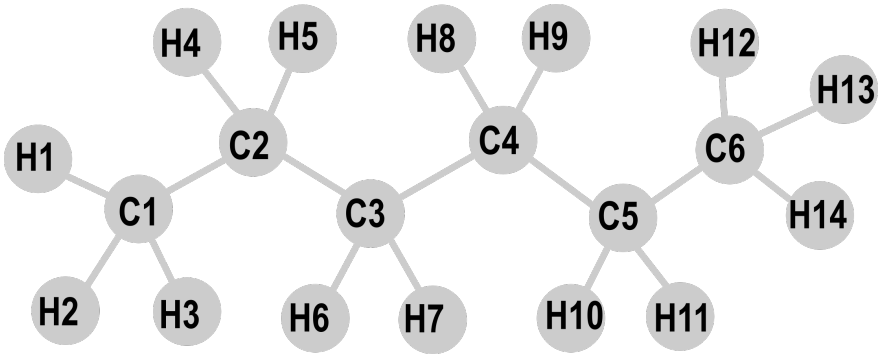

Figure S9: Atom names of *n*-hexane molecule in the force field.

Table S8: Parameters for the non bonded interactions of the n-hexane molecule. C_6 and C_{12} are the parameters of the Lennard Jones interactions.

Index	Atom name	Atom type	Mass (Da)	Charge (e)	C_6 (kJ mol^{-1} nm^6)	C_{12} (kJ mol^{-1} nm^{12})
1	H14	HC	1.0080	0.069	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
2	C6	C	12.0110	-0.309	0.0023406244	$4.937284 \cdot 10^{-6}$
3	H12	HC	1.0080	0.069	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
4	H13	HC	1.0080	0.069	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
5	C5	C	12.0110	0.219	0.0023406244	$4.937284 \cdot 10^{-6}$
6	H10	HC	1.0080	-0.037	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
7	H11	HC	1.0080	-0.037	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
8	C4	C	12.0110	-0.057	0.0023406244	$4.937284 \cdot 10^{-6}$
9	H8	HC	1.0080	0.007	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
10	H9	HC	1.0080	0.007	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
11	C3	C	12.0110	-0.057	0.0023406244	$4.937284 \cdot 10^{-6}$
12	H6	HC	1.0080	0.007	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
13	H7	HC	1.0080	0.007	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
14	C2	C	12.0110	0.219	0.0023406244	$4.937284 \cdot 10^{-6}$
15	H4	HC	1.0080	-0.037	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
16	H5	HC	1.0080	-0.037	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
17	C1	C	12.0110	-0.309	0.0023406244	$4.937284 \cdot 10^{-6}$
18	H1	HC	1.0080	0.069	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
19	H2	HC	1.0080	0.069	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$
20	H3	HC	1.0080	0.069	$8.464 \cdot 10^{-5}$	$1.5129 \cdot 10^{-8}$

Table S9: Bond-stretching parameters of the n-hexane molecule.

Atom 1	Atom 2	Equilibrium bond length (nm)	Force constant (kJ mol^{-1} nm^{-4})
H14	C6	0.1090	$1.2300 \cdot 10^7$
C6	H12	0.1090	$1.2300 \cdot 10^7$
C6	H13	0.1090	$1.2300 \cdot 10^7$
C6	C5	0.1530	$7.1500 \cdot 10^6$
C5	H10	0.1090	$1.2300 \cdot 10^7$
C5	H11	0.1090	$1.2300 \cdot 10^7$

C5	C4	0.1530	$7.1500 \cdot 10^6$
C4	H8	0.1100	$1.2100 \cdot 10^7$
C4	H9	0.1100	$1.2100 \cdot 10^7$
C4	C3	0.1530	$7.1500 \cdot 10^6$
C3	H6	0.1100	$1.2100 \cdot 10^7$
C3	H7	0.1100	$1.2100 \cdot 10^7$
C3	C2	0.1530	$7.1500 \cdot 10^6$
C2	H4	0.1090	$1.2300 \cdot 10^7$
C2	H5	0.1090	$1.2300 \cdot 10^7$
C2	C1	0.1530	$7.1500 \cdot 10^6$
C1	H1	0.1090	$1.2300 \cdot 10^7$
C1	H2	0.1090	$1.2300 \cdot 10^7$
C1	H3	0.1090	$1.2300 \cdot 10^7$

Table S10: Angle bending parameters of the *n*-hexane molecule.

Atom 1	Atom 2	Atom 3	Equilibrium angle (degree)	Force constant (kJ mol^{-1})
H14	C6	H12	107.57	484.00
H14	C6	H13	107.57	484.00
H14	C6	C5	111.40	532.00
H12	C6	H13	107.57	484.00
H12	C6	C5	111.40	532.00
H13	C6	C5	111.40	532.00
C6	C5	H10	109.50	448.00
C6	C5	H11	109.50	448.00
C6	C5	C4	111.00	530.00
H10	C5	H11	106.75	503.00
H10	C5	C4	109.50	448.00
H11	C5	C4	109.50	448.00
C5	C4	H8	109.50	448.00
C5	C4	H9	109.50	448.00
C5	C4	C3	111.00	530.00
H8	C4	H9	106.75	503.00
H8	C4	C3	109.50	448.00
H9	C4	C3	109.50	448.00

C4	C3	H6	109.50	448.00
C4	C3	H7	109.50	448.00
C4	C3	C2	111.00	530.00
H6	C3	H7	106.75	503.00
H6	C3	C2	109.50	448.00
H7	C3	C2	109.50	448.00
C3	C2	H4	109.50	448.00
C3	C2	H5	109.50	448.00
C3	C2	C1	111.00	530.00
H4	C2	H5	106.75	503.00
H4	C2	C1	109.50	448.00
H5	C2	C1	109.50	448.00
C2	C1	H1	111.40	532.00
C2	C1	H2	111.40	532.00
C2	C1	H3	111.40	532.00
H1	C1	H2	107.57	484.00
H1	C1	H3	107.57	484.00
H2	C1	H3	107.57	484.00

Table S11: Proper dihedral angle parameters of the *n*-hexane molecule.

Atom 1	Atom 2	Atom 3	Atom 4	Equilibrium proper dihedral angle (degree)	Force constant (kJ mol^{-1})	Multiplicity
C6	C5	C4	C3	0.00	5.92	3
H12	C6	C5	C4	0.00	5.92	3
C5	C4	C3	C2	0.00	5.92	3
C4	C3	C2	C1	0.00	5.92	3
C3	C2	C1	H1	0.00	5.92	3

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